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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,762	11/27/2001	Graeme Milligan	9013-13	5290

20792 7590 07/16/2004

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
913762	MILLIGAN
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 4/6/04.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-2, 5-9, 12-24, 26-29, 32 is/are pending in the application.

Of the above claim(s) 27-29, 32 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-2, 5-9, 12-24, 26 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

Amendment of 4/8/04 has been entered. Claims 1-2, 5-9, 12-24, 26-29 and 32 are pending. Claims 1-2, 5-9, 12-24 and 26 are under examination.

The disclosure is objected to because of the following informalities: in substituted page 31, penultimate line, insertion of "agonist ligand" is redundant.

Appropriate correction is required.

Regarding 112, second paragraph rejections of record, the amendment has overcome previously stated issues pertaining to claims 1, 4-6, 8, 12, 14-16 and 18-20. Examiner concurs that claims 22-23 do not recite "or the like" and "such as."

The following 112 rejection of record is maintained.

Claims 24 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 24 the preamble recites "compound" while steps c) and d) recite "test compound". Consistency is required.

Examiner considers that claim 7 further limits base claim 1, since the Markush group members of claim 7 do not exhaustively describe all compounds that could be used in claim 1. For example, there are also "partial agonists" (Liaw et al, col.7, line 40).

The amendment and urgings have overcome previously stated prior art rejections. The examiner concurs that Leurs et al do not motivate one to use a constitutively active mutant receptor in the assay systems of Barak et al or Siegel et al.

Due to the finding of a new reference, a new ground of prior art rejection is stated below.

Claims 1, 2, 6-9, 13-17, 20-22 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Barak et al and Siegel et al in view of Liaw et al (6,555,339).

Barak et al have been previously cited against original claim 1 and dependent claims 8-10, 13-17, 20-22 and 24. It is presently noted that they teach use of cells that express a fusion protein having a beta-2 andrenergic receptor and GFP reporter segments. It is also noted that they teach that the beta-2 andrenergic receptor is a G-protein coupled receptor (GPCR) and that their method can be used for the study of other GPCRs (abstract; page 183, col.2; page 184, col.1).

Siegel et al, were previously cited against original claims 1 and 24 and dependent claims 2-3, 6-9, 13-17 and 20. Presently, the examiner notes that they teach that use of a receptor-reporter fusion polypeptide that yields an optically detectable signal--e.g from GFP as taught by Barak et al--provides for a particularly convenient and sensitive read-out of assay results (page 5, lines 13+; page 15, lines 1+).

Liaw et al teach production of constitutively active GPCRs obtained by mutation ("non-endogenous" essential means "mutant"; see col.8, lines 51+); they teach that cells expressing such receptors, can be used in drug screening assays (col.4, lines 28-35; col.6, lines 5-39) and for understanding the role of the receptors in signaling events (col.14, line 59-col.15, line 9) they teach that it is advantageous for one to use receptors that are constitutively active in such screening assays because one can identify

candidate agonists, antagonists, etc without knowledge of what the "endogenous" (i.e. native) ligand of an orphan CPCR may be (e.g. col.6, lines 31+; col.10, lines 64-68. Because the GFP readout assay systems of Barak et al and Siegel et al are particularly convenient for conducting screening assays, or for observing the biological changes that occur within a cell upon ligand binding, and because the use of constitutively activate mutant forms of a receptor allow one to conduct screening assays or monitor biological events without the need for one to know the identity of the native ligand of an orphan receptor, one would have been fully motivated to modify the assay systems of Barak et al or Seigel et al by using a mutant, constitutively active form of receptor segment, in lieu of the wild form of such segment; at the least, this motivation would hold in the case in which the receptor is an orphan receptor having no identified native ligand. Thus claims 1 and 24 would have been obvious. Dependent claims are rejected as previously noted regarding Barak et al and Seigel et al. --i.e. for claims 2, 6-9, 13-17, 20-22 and 24.

Claims 5, 12 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barak et al and Seigel et al in view of Liaw et al. as applied to claims 1-2 and 24 above, and further in view of Leurs et al.

Leurs et al are relied upon for teaching the feature that, when an inverse agonist binds to a constitutively active mutant (CAM) form of a CPCR, there will be an increase in receptor activity, as in claims 12 and 26; note, as set forth above, Liaw et al are relied upon for motivating use of a CAM receptor segment. Leurs et al have also been previously noted for teaching limitations of claim 5.

Claims 18-19 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barak et al and Seigel et al in view of Liaw et al. as applied to claim 1 above, and further in view of Bryan et al.

Bryan et al, as previously noted, teach that luciferase and GFP reporters may be used interchangeably and that assays may be conducted in multiwell plates.

Applicant's arguments with respect to claims 1-2, 5-8, 12-24 and 26 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Monday-Thursday from 8:00a.m to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182/644

Saunders/tgd

June 30, 2004